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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,867	03/15/2001	Michael John Bradley Kutryk	1133279-0003	5578

7470 7590 04/07/2004

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EXAMINER	
CHATTOPADHYAY, URMI	
ART UNIT	**PAPER NUMBER**
3738	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,867	KUTRYK ET AL.	
	Examiner	Art Unit	
	Urmi Chattopadhyay	3738	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42,45,46,48 and 51-61* is/are pending in the application.

4a) Of the above claim(s) *6,10-17,19,26,33-37,40,42,46,48 and 51-55* is/are withdrawn from consideration.

5)☒ Claim(s) *41 and 45* is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-9,18,20-25,27,29-32,38,39 and 56-61* is/are rejected.

7)☒ Claim(s) *3 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 1/16/04 has been entered. Claims 43, 44, 47, 49 and 50 have been canceled and new claims 56-61 have been added. Claims 6, 10-17, 19, 26, 33-37, 40, 42, 46, 48 and 51-55 remain withdrawn from consideration for being drawn to non-elected species. The claims being considered for further examination on the merits are 1-5, 7-9, 18, 20-25, 27-32, 38, 39, 41, 45 and 56-61.

2. As applicant pointed out in on page 10 of the amendment, there was an error in the previous office action (mailed 7/16/03). Claim 2 was indicated as containing allowable subject matter, when in fact it was rejected under 35 U.S.C. § 103. The examiner intended to indicate claim 3 has containing allowable subject matter.

Information Disclosure Statement

3. The Information Disclosure Statement filed 2/13/04 has been entered. All references cited therein have been considered. An initialed copy of the PTO-1449 is enclosed.

Oath/Declaration

4. The Supplemental Declaration filed 2/13/04 has been entered and approved by the examiner.

Specification

5. The specification is objected to. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The word "invention" on line 1 is legal phraseology that needs to be removed. The examiner suggests changing the first sentence to --Compositions and methods for producing a medical device coated with a matrix and an antibody which reacts with an endothelial cell antigen are disclosed.--

Claim Objections

6. Claims 38, 56 and 57 are objected to because of the following informalities:

a. Claim 38, line 2, "a" before "medical device" should be deleted.

b. Claims 56 and 57 appear to be the same as claims 18 and 20, respectively. See 112, second paragraph rejection below for further explanation. They should be canceled.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 56 is indefinite because it is unclear if the medical device is being claimed as part of the invention or not. The examiner appreciates applicant's intention of rendering moot the "intended use" of the composition. However, in order to structurally claim the medical device, the claims should be rewritten as a combination claim, without duplicating any existing claim. For examination purposes, the device is not being considered a part of the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 4, 7, 9, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. (*Improved Adhesion and Proliferation of Human Endothelial Cells on Polyethylene Precoated with Monoclonal Antibodies Directed Against Cell Membrane Antigens and Extracellular Matrix Proteins*, as cited in applicant's IDS) in view of Richmond et al. (USPN 5,310,669 as cited in applicant's IDS).

Dekker et al. discloses a coated medical device and method for treating mammals for obstruction of a vessel with all the elements of claims 1 and 38, but is silent to the medical device being coated with at least one layer of a matrix comprising fullerene ranging from about

C60 to about C100. See *Summary* and *Introduction* for treating mammals for obstruction of a vessel using a medical device (vascular graft) coated with a therapeutically effective amount of at least one type of antibody, which reacts with an endothelial cell antigen. Richmond et al. teaches a substrate coated with a matrix comprising fullerene C60 with an antibody bound thereto (claim 2; column 5, lines36-37) in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. See column 3, lines 31-35 and columns 3-4, lines 65-19. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Richmond et al. to modify the method of Dekker et al. by including to the medical device antibody coating at least one layer of matrix comprising a fullerene of about C60 in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content.

Claims 4 and 9, see *Summary* for antibody being the monoclonal antibody, $F(ab')_2$ fragments.

Claim 7, see pages 716-717 under *Cell Adhesion and Proliferation* for human endothelial cells.

Claim 39, see line 2 of *Introduction* for vessel being an artery.

10. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. and Richmond et al. as applied to claim 1 above, and further in view of Watson et al. (USPN 5,688,486).

Dekker et al., as modified by Richmond et al., discloses a coated medical device with all the elements of claim 1, but is silent to the medical device being a stent. Watson et al. teaches a stent coated with a fullerene ranging from about C60 to about C100 in order to provide the stent with singlet oxygen generators. See column 17, lines 55-63. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Watson et al. to coat a stent with the coating of Dekker et al. in order to provide the stent with singlet oxygen generators. These generators are useful particularly in the areas where stents are required in the process of studying cell membrane composition e.g., cholesterol content.

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. and Richmond et al. as applied to claims 1 and 4 above, and further in view of Asahara et al. (*Isolation of Pututive Progenitor Endothelial Cells for Angiogenesis*, as cited in applicant's IDS).

Dekker et al., as modified by Richmond et al., discloses a coated medical device with all the elements of claim 1, but is silent to the monoclonal antibody reacting with endothelial cell surface antigen CD34, as required by claim 8. Asahara et al. teaches, as disclosed by applicant on page 15 of the specification, using anti-CD34 monoclonal antibodies attached to a solid support in order to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Asahara et al. to modify the monoclonal antibody of Dekker et al. and Richmond et al. so that it reacts with the endothelial cell surface antigen CD34 in order for it to capture progenitor endothelial cells that are capable of

differentiating into endothelial cells. This increases endothelial cell proliferation and graft patency.

12. Claims 18, 20-22, 24, 25, 27, 56-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richmond et al. in view of Dekker.

Richmond et al. discloses a composition and method of coating a substrate with all the elements of claims 18, 25 and 56, but is silent to the antibody reacting with an endothelial cell antigen and the substrate being a medical device. See abstract and column 5, lines 24-37 for a composition that is capable and suitable of being coated to a medical device (the word "for" is intended use language only and the medical device is not a part of the claimed invention) and method for coating a substrate comprising a matrix (fullerene) and a therapeutically effective amount of at least one type of antibody bound thereto (claim 27). Dekker et al. teaches coating a medical device (vascular graft) with mixtures of monoclonal antibody $F(ab')_2$ fragments (claims 21, 24, 58 and 61) that react with a human endothelial cell antigen (claims 22 and 59) in order to promote growth and proliferation of endothelial cells and improve the patency of graft. See *Summary* on page 715 and *Cell Adhesion and Proliferation* on pages 716-717. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Dekker et al. to make the substrate of Richmond et al. a medical device and the antibody monoclonal antibody $F(ab')_2$ fragments that react with a human endothelial cell antigen in order to promote growth and proliferation of endothelial cells and improve graft patency.

Claims 20 and 57, see column 3, lines 8-14 for fullerene within the required range.

13. Claims 23 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richmond et al. and Dekker et al. as applied to claims 21 and 56 above, and further in view of Asahara et al.

Richmond et al., as modified by Dekker et al., discloses a composition with all the elements of claims 21 and 56, but is silent to the monoclonal antibody reacting with endothelial cell surface antigen CD34, as required by claims 23 and 60. Asahara et al. teaches, as disclosed by applicant on page 15 of the specification, using anti-CD34 monoclonal antibodies attached to a solid support in order to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Asahara et al. to modify the monoclonal antibody of Richmond et al. and Dekker et al. so that it reacts with the endothelial cell surface antigen CD34 in order for it to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. This increases endothelial cell proliferation and graft patency.

14. Claims 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. in view of Richmond et al. and Bos et al. (*Small-Diameter Vascular Graft Prosthesis: Current Status*, as cited in applicant's IDS).

Dekker et al. discloses a method for treating mammals with obstructed arteries with all the elements of claim 29, but is silent to the method specifically treating for atherosclerosis and the medical device being coated with at least one layer of a matrix comprising fullerene ranging from about C60 to about C100. See *Summary* and *Introduction* for treating mammals for

obstruction of a vessel using a medical device (vascular graft) coated with a therapeutically effective amount of at least one type of antibody, which reacts with an endothelial cell antigen. Richmond et al. teaches a substrate coated with a matrix comprising fullerene C60 with an antibody in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. See column 3, lines 31-35 and columns 3-4, lines 65-19. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Richmond et al. to modify the method of Dekker et al. by including to the medical device antibody coating at least one layer of matrix comprising a fullerene of about C60 in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. Bos et al. teaches that it is old and well known in the art to treat mammals for atherosclerosis with grafts under *Introduction* (first paragraph). It would have been obvious, therefore, to one of ordinary skill in the art to use the graft of Dekker et al. to treat atherosclerosis, specifically in the coronary artery (claim 31), because it is customary to do so.

Claims 30 and 32, see *Summary* of Dekker et al. for antibody being the monoclonal antibody $F(ab')_2$ fragments.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 18, 25, 27, 29-31, 38, 39, 56, 58, 60 and 61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10, 27, 32, 33, 35, 37, 42, 45, 47 and 49 of copending Application No. 10/360,567. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the current application include all of the limitations of those of the copending application and are broader in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

17. Claims 41 and 45 are allowed.

18. Claims 3 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

19. Applicant's arguments filed 1/16/04 have been fully considered but they are not persuasive.

Applicant's arguments are directed against the Dekker et al. reference, which was used in combination with at least one other reference in each of the §103 rejections. Applicant argues that the express intent, purpose and function of the Dekker study require the use of a "matrix-free" polyethylene graft as the model substrate. The examiner disagrees. In the study, polyethylene was chosen as the model substrate because adhesion onto the uncoated surface is low. When the polyethylene substrate is coated with F(ab')2 fragments of monoclonal antibodies directed against endothelial cell specific membrane antigens in combination with monoclonal antibodies directed against extracellular matrix proteins, growth and proliferation of endothelial cells and limited platelet deposition is seen. This was an improvement over the fibronectin coated polyethylene (endothelial cells adhered, but did not proliferate and platelet reactivity was significant). While the study did not include a matrix to the surface of the polyethylene, the intent, purpose and function of the study was to see how a precoating with monoclonal antibodies directed against cell membrane antigens and extracellular matrix proteins would be an improvement over other coatings. The inclusion of a matrix to the polyethylene substrate would not destroy the intent, purpose or function of the study, because the ability of the monoclonal antibodies directed against cell membrane antigens and extracellular matrix protein to provide the polyethylene with optimal endothelial cell adhesion and proliferation with negligible platelet activity would not be affected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Urmi Chattopadhyay whose telephone number is (703) 308-8510 and whose work schedule is Monday-Friday, 9:00am – 6:30pm with every other Friday off. The examiner's supervisor, Corrine McDermott, may be reached at (703) 308-2111. The group receptionist may be reached at (703) 308-0858.

Should the applicant wish to send a fax for official entry into the file wrapper the Group fax number is (703) 872-9306. Should applicant wish to send a fax for discussion purposes only, the art unit fax number is (703) 308-2708.

Urmi Chattopadhyay

Art Unit 3738

David J. Isabella
Primary Examiner